PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference H 2095 PCT S3	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/EP 03/06766	International filing date *(day/month/year)* 26.06.2003	Priority date *(day/month/year)* 08.07.2002
International Patent Classification (IPC) or both national classification and IPC G01N33/68		
Applicant GENOVA, LTD. et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
04.02.2004	18.08.2004
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Giry, M Telephone No. +49 89 2399-7328

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP 03/06766

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-91 as originally filed

Sequence listings part of the description, Pages

1-7 as originally filed

Claims, Numbers

1-13 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).

   ☐ the language of publication of the international application (under Rule 48.3(b)).

   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☒ contained in the international application in written form.

   ☒ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority in written form.

   ☐ furnished subsequently to this Authority in computer readable form.

   ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:

   ☐ the claims, Nos.:

   ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-6, 12
	No:	Claims	7-11, 13
Inventive step (IS)	Yes:	Claims	1-6
	No:	Claims	7-13
Industrial applicability (IA)	Yes:	Claims	1-13
	No:	Claims	

2. Citations and explanations

   see separate sheet

Re Item V

Reasoned statement under Art. 35(2) PCT with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1 - **Reference** is made to the following documents :

D1: WO 99 31236 A, 24 June 1999
D2: WO 02 18623 A, 7 March 2002

2 - **Novelty** - Art. 33(1) and (2) PCT :

2.1 Document D1 discloses the sequences of extended cDNAs encoding secreted proteins. In particular, the protein identified by SEQ ID NO: 225 is a phosphoethanolamine binding protein (PEBP) family member which presents over 99.5 % identity with SEQ ID NO:2 of the present application (p. 93, lines 22-32 ; p. 136, Table VIII). Document D1 discloses a purified protein comprising said sequence (claim 9) and a purified antibody specific for the protein having said sequence (claim 17). The fusion of said protein to a heterologous protein sequence is also contemplated (p. 65, lines 1-10). Said antibodies, which can be directly of indirectly conjugated to a detectable marker, are used in immunoassays to determine concentrations of antigen-bearing substances in biological samples (p. 66-67, Example 40 , p. 71, Example 48).
Document D1 is therefore novelty destroying for the subject-matter of present claims 7-11.

2.2 Document D2 discloses methods for identifying modulators of a biological activity of a PEBP family member (p. 7, last paragraph ; p. 33-34, claims 10 and 14) which anticipate the subject-matter of present claim 13.

3 - **Inventive step** - Art. 33(1) and (3) PCT :

3.1 In view of the available prior art documents the problem to be solved by the subject-matter of claims 1-6 can be seen in providing methods for diagnosing / predicting a cardiovascular disorder. This problem is solved by determining in a biological sample of a subject an increase in the level of a member of the PEBP family identified by the SEQ ID NO: 2 or 4.

None of the available prior art documents suggests a correlation between an *elevated* level of PEBP peptide in a biological sample with a *cardiovascular* disorder.
The subject-matter of claims 1-6 can therefore be considered as involving an inventive step.

3.2 The subject-matter of claim 12 lacks an inventive step since it would be an obvious step for the person skilled in the art to contemplate the performance of the known method of claim 10 in human plasma.

4 - **Industrial applicability** - Art. 33(1) and (4) PCT :

The subject-matter of claims 1-13 appears to be industrially applicable.